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Effect of smoking a single cigarette on the "small airways"

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DA SILVA, ANGELO M. T., AND PAUL HAMOSH. *Effect of smoking a single cigarette on the "small airways."* J. Appl. Physiol. 34(3): 361–365. 1973.—We studied the effect of smoking one cigarette on lung function in 21 healthy subjects. Airway resistance measured by body plethysmography increased in 19 patients. "Closing volume," breath-by-breath nitrogen washout and frequency dependence of dynamic compliance (in 7 patients) were not significantly changed after smoking a cigarette. The maximum expiratory flow at 50% of the vital capacity (MEF_{50}) decreased significantly. These later measurements are currently used for assessment of the function of "small airways" (less than 2 mm in diameter). These findings indicate that smoking a cigarette does not increase "small airway" resistance measurably, when procedures not requiring maximum expiratory flow are used. On the other hand, the decrease of MEF_{50} after a maximum expiratory flow-volume maneuver indicates that airways upstream from the flow limiting segment have increased resistance after smoking a cigarette, since no changes in the elastic properties of the lung were demonstrated.

airway resistance; compliance; "closing volume"; flow-volume curve

SMOKING A CIGARETTE increases airway resistance (Raw) (2, 3, 6, 8, 21, 23, 25, 26, 27, 31). This response is mediated by the vagus and suppressed by isuprel and atropine (23, 27, 31). Most studies have been done before the importance of the "small airways" was fully appreciated (13). The "small airways" contribute only 10 to 30 per cent to the total airway resistance and therefore constitute a "silent area" of the lung (16, 20, 30). Determination of the frequency dependence of dynamic compliance (30), "closing volume" (1, 10) and analysis of the maximum expiratory flow volume curve (4) are methods recently introduced to assess "small airway" function. We report the acute effect of cigarette smoke on these measurements.

MATERIALS AND METHODS

Twenty-one subjects were studied (Table 1). Of these, 17 were healthy hospital employees, the rest were outpatients in an alcoholic clinic with no evidence of organic disease. The smokers abstained from cigarettes for two hours prior to the measurements. Thoracic gas volume (Vtg) at functional residual capacity (FRC) and the Raw were measured by the method of DuBois et al. (11, 12) using a constant-volume plethysmograph (Warren E. Collins, Inc., Braintree, Mass.). The "closing volume" (CV) was determined by the single-breath nitrogen washout method (1). After completion of this procedure maximum expiratory flow-volume curves (MEFV) were obtained in a volume displacement plethysmograph (Med-Science Electronics, St. Louis, Mo.). The flow was measured with a Fleisch pneumotachograph and a Sanborn 270 differential pressure transducer. The volume signal from the plethysmograph and the flow signal were displayed, respectively, on the horizontal and vertical axes of a storage oscilloscope (Tektronix, Inc., 564B) and photographed. The maximum expiratory flows at the moments when 50% of the vital capacity had been expelled (MEF_{50}) and when 75% had been expelled (MEF_{75}) were read directly from the flow-volume curve. All measurements were made five times and averaged.

Following these procedures, the subjects smoked a non-filter cigarette containing 25 mg tar and 1.5 mg nicotine per g of cigarette (9) in approximately 5 min. Procedures were repeated immediately after the subject finished smoking.

On a separate occasion breath-by-breath nitrogen washout was measured before and after smoking. Lung compliance was measured in seven subjects at different respiratory frequencies (26). Transpulmonic pressure was measured by an esophageal balloon (22) and lung volume by the volume displacement body plethysmograph. Statistical analysis was done using the paired *t* test.

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RESULTS

The clinical data on the experimental subjects is summarized in Table 1. The age ranged from 25 to 49 with a mean of 33.3 years. Nine out of the twenty-one were active smokers at the time of the study. Only three subjects had never smoked. Nine subjects quit smoking between 1 and 10 years prior to the time of investigation. Five subjects fulfilled the criteria for chronic bronchitis (7).

The results of the respiratory function tests are summarized in Table 2. The vital capacity did not change significantly after smoking. The FRC showed only very small changes. The "closing volume" was determined in 18 subjects and did not show significant changes. Airway resistance increased in 19 of the 21 subjects and the change was statistically highly significant ($P < 0.001$). Conductance and specific conductance both decreased significantly. Since there was not significant increase in FRC after smoking we did not find the specific conductance a more useful expression than conductance itself. Maximum expiratory flow

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TABLE 1. *Clinical information on 21 subjects*

Subj	Age, yr	Wt, kg	Smoking History				Clincal Signs		
			At present	If quit, when? yr	Cigarettes/ day	Duration, yr	Cough	Sputum	Duration
NN	31	69	Never						
SR	31	69	Quit	3	20	9			
SL	32	75	Quit	10	40	7			
GG	28	70	Quit	4	10	3			
LJ	31	82	Never						
ME	34	89	Yes		40	17			
DA	33	75	Quit	2	15	15			
HP	40	72	Quit	4	20	17			
SS	31	91	Quit	4	40	10			
NR	31	75	Quit	3	20	13			
CL	32	58	Quit	1	20	12			
PJ	29	77	Yes		20	7			
JE	32	72	Never						
AO	30	64	Quit	3	20	10			
CR	45	75	Yes		40	25	+	+	More than 2 yr
RT	40	73	Yes		40	12	+	+	More than 2 yr
OA	49	86	Yes		50	35	+	+	More than 2 yr
SJ	37	84	Yes		20	19	+	+	Less than 2 yr
GP	25	65	Yes		30	10	+	+	More than 2 yr
MR	26	69	Yes		20	7	+	+	Less than 2 yr
RH	33	56	Yes		30	13	+	+	More than 2 yr
Mean	33.33	73.76							
± SD	±5.91	±9.39							

TABLE 2. *Pulmonary function tests before and after smoking a cigarette*

Subj	VC, liters		FRC, liters		CV, % of VC		Raw, cm H_2O/ liter per sec		Gaw, liter/sec per cm H_2O		SGaw, liter/sec per cm H_2O/ liter lung vol		MEF liter/sec		MEF_{50}, liter/sec		MEF_{75}, liter/sec		Cdyn, liter/cm H_2O	
	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A
NN	5.0	5.0	3.66	3.70	7.5	8.6	1.06	1.27	0.95	0.79	0.26	0.21	8.8	8.6	6.3	5.4	3.3	3.0		
SR	3.9	4.0	2.43	2.56	11.5	11.1	1.26	1.33	0.79	0.75	0.33	0.29	11.0	10.5	6.6	6.0	3.3	3.3		
SL	4.7	4.6	2.49	2.42	11.0	10.6	1.79	1.79	0.56	0.56	0.22	0.23	8.6	8.7	5.3	4.5	2.1	2.0	0.20	0.19
GG	4.6	4.5	3.79	3.75	12.5	11.3	1.27	1.38	0.79	0.72	0.21	0.19	9.9	9.1	4.8	4.5	2.4	2.4	0.21	0.20
LJ	4.2	4.1	2.27	2.15	12.0	11.3	1.32	1.48	0.76	0.67	0.33	0.31	11.5	11.5	5.7	4.8	2.2	2.8	0.19	0.19
ME	4.4	4.1	3.49	3.61	13.2	13.5	1.16	1.12	0.86	0.89	0.25	0.25	11.0	10.7	6.7	6.1	1.6	1.8		
DA	5.0	5.0	4.73	4.36	10.6	10.7	1.06	1.34	0.94	0.75	0.20	0.17	11.0	10.5	5.8	5.7	2.8	3.0	0.20	0.20
HP	4.6	4.5	3.18	3.03	15.3	15.3	0.86	0.93	1.17	1.07	0.37	0.35	9.0	9.1	6.0	6.0	2.4	2.5		
SS	5.0	5.0	3.29	3.01	12.6	15.5	1.26	1.62	0.80	0.62	0.24	0.21	8.7	8.7	5.0	4.6	2.1	2.1		
NR	4.6	4.2	3.66	3.66	8.5	7.1	1.10	1.14	0.91	0.88	0.25	0.24	7.5	7.5	4.9	5.1	2.2	2.5		
PJ	4.5	4.4	2.66	2.57			1.36	1.51	0.73	0.66	0.27	0.25	9.6	8.5	6.3	5.7	3.0	2.7		
CL	4.0	4.0	3.78	3.62	14.3	15.8	1.25	1.48	0.80	0.67	0.21	0.18	7.2	6.6	5.7	5.1	3.5	2.7		
JE	4.2	4.3	4.54	4.58			1.47	1.35	0.68	0.74	0.15	0.16	9.6	9.6	6.2	6.0	5.1	5.0		
AO	4.8	4.6	4.63	4.42			1.02	1.16	0.98	0.86	0.21	0.19	10.5	9.6	6.9	6.9	4.1	5.0		
CR	3.2	3.0	2.93	2.96	29.0	27.0	1.70	1.78	0.59	0.56	0.20	0.18	6.0	6.0	3.3	3.3	1.2	1.3		
RT	3.5	3.6	3.74	3.83	23.0	22.0	1.21	1.31	0.83	0.76	0.22	0.20	9.0	8.7	5.1	4.8	2.5	2.1	0.21	0.22
OA	4.6	4.6	3.57	3.61	27.0	25.0	1.24	1.36	0.81	0.73	0.23	0.20	9.0	7.5	7.2	6.7	3.3	3.0		
SJ	3.7	3.6	3.41	3.45	26.0	24.0	1.46	1.65	0.68	0.60	0.20	0.17	9.3	8.1	4.0	4.1	1.4	1.4		
GP	4.9	4.8	3.56	3.62	14.0	13.0	1.25	1.53	0.80	0.65	0.22	0.18	8.2	7.8	3.6	3.4	1.5	1.5	0.18	0.20
MR	5.6	5.8	3.41	3.37	8.5	8.5	1.57	1.83	0.64	0.55	0.19	0.16	8.2	8.1	5.1	4.8	3.0	2.6		
RH	4.9	5.0	3.53	3.66	15.0	15.0	1.42	1.57	0.70	0.64	0.19	0.17	7.5	7.5	4.0	3.7	1.9	1.7	0.22	0.22
Mean	4.47	4.41	3.46	3.42	15.0	14.7	1.29	1.42	0.79	0.72	0.24	0.21	9.1	8.7	5.5	5.1	2.6	2.6	0.20	0.20
± SD	0.56	0.60	0.66	0.64	6.59	5.97	0.20	0.22	0.10	0.10	0.05	0.05	1.41	1.37	1.09	1.0	0.94	0.94	0.01	0.01
Mean % change					−1.17		+10.93		−9.49		−9.3		−4.15		−6.07		−0.12		+1.55	

VC = vital capacity; FRC = functional residual capacity; CV = closing volume; Raw = airway resistance; Gaw = airway conductance; SGaw = specific airway conductance; MEF = maximum expiratory flow; MEF_{50} = MEF at 50% of vital capacity; MEF_{75} = MEF at 75% of vital capacity; Cdyn = dynamic compliance. B = before smoking a cigarette; A = after smoking a cigarette.

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showed a mean decrease of 4.15% but this change was not significant. MEF_{50} decreased by 6.07% and this change was statistically highly significant ($P < 0.001$). MEF_{75} remained unchanged but tended to be low in patients who fulfilled the clinical criteria for chronic bronchitis. The dynamic compliance was within normal limits in all subjects and did not significantly change after smoking.

The relationship between dynamic lung compliance and frequency of breathing is shown in Figs. 1 and 2. Only *subject GP* exhibited frequency dependence of compliance. None of the seven subjects showed significant changes in this relationship before and after smoking.

Breath-by-breath nitrogen washout was performed before and after smoking in 17 of the 21 subjects. The results were plotted on semilogarithmic paper. Sixteen out of the seventeen subjects had linear washout curves. *Subject GP* had a nonlinear curve. Smoking did not affect significantly the time course and linearity of these curves in any of the subjects. The heart rate was measured before and after smoking the cigarette to assess the circulatory effect. Mean heart rate before smoking was 81 beats/min and after smoking 88. Most active smokers did not respond with increase in heart rate, whereas some nonsmokers showed up to 50% increase in heart rate.

DISCUSSION

The effect of acute inhalation of cigarette smoke on lung volumes and airway resistance has been studied by Nadel and Comroe (23) and others (8, 25, 26). The results of this study are only different in the magnitude of the changes. An increase in airways resistance was clearly demonstrated, but the changes in FRC were not significant. The smaller changes are probably due to the fact that each determination was preceded by a deep inspiration to insure uniform volume history. Deep inspiration is known to reduce airway resistance (24). The airway resistance increased in 19 of 21 subjects. This increase in airway resistance is probably due to constriction of the large airways (28). The method used for determination of the Raw is not sensitive enough for measurement of "small airway" resistance (13, 16, 30). Direct measurements of small airway resistance in humans is impossible since it requires partitioning of the pressure drop in the airways at a point in the bronchial tree that is inaccessible to direct measurements (13, 16). Retrograde catheterization in dogs has shown that airways less than 2mm in diameter contribute only about twenty percent of the total airway resistance (16). Theoretically, a two-to-three-fold increase in small airway resistance could remain undetected.

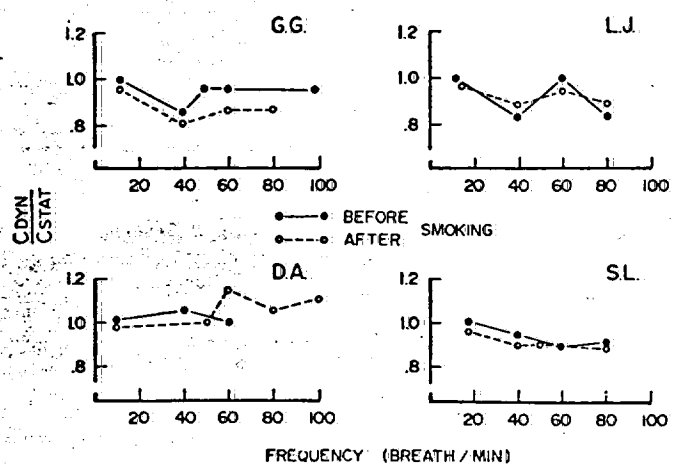

FIG. 1. Relationship between the ratio of dynamic to static compliance and frequency of breathing before and after smoking a cigarette in four nonsmokers.

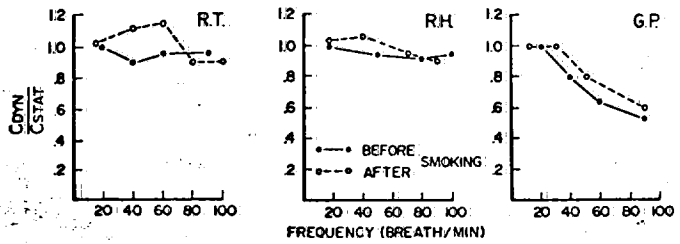

FIG. 2. Relationship between the ratio of dynamic to static compliance and frequency of breathing before and after smoking a cigarette in three smokers.

Subjects with chronic cough or heavy cigarette smokers have shown frequency dependent dynamic compliance (15, 19, 30), abnormal distribution of air at increasing respiratory frequency (17), abnormal nitrogen washout curves at high respiratory rates (14) and a reduction in mid-expiratory flow (19). Therefore it has been suggested that the earliest pathologic changes in chronic obstructive pulmonary disease occur in these small airways (13).

Dynamic compliance of the lung (Cdyn) in normal subjects is independent of the frequency of breathing (30) at least to 80 cycles/min. It has been reported that Cdyn becomes frequency dependent in early lung disease before airways resistance and flow rates show impairment (14, 15, 19, 30). In a recent study, chronic smokers showed a larger incidence of frequency dependence of dynamic compliance than nonsmokers (15). The dynamic compliance may become frequency independent again after discontinuing cigarette smoke (15, 19). These observations indicate an early involvement of the small airways in smokers. Our study shows that smoking one cigarette did not change the relationship between dynamic lung compliance and frequency of breathing in seven subjects. A number of mechanisms can be advanced to explain why Cdyn did not become frequency dependent. Since the bronchoconstrictor effect of cigarette smoke is related mostly to concentration of particulate matter (8), it is possible that a concentration gradient exists along the bronchial tree and particles do not reach the small airways in concentrations high enough to cause acute constriction. A nonuniform effect of the smoke in different areas of the lung will also be necessary to produce frequency dependence of dynamic compliance. If the effect is small and all airways were affected uniformly, the dynamic compliance should not become frequency dependent. The absence of response might also be a result of collateral ventilation. Dogs have large collateral ventilation and peripheral airway resistance can increase without causing frequency dependence of compliance (29). Man has less collateral ventilation than the dog, but significant variability might exist.

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Breath-by-breath nitrogen washout was suggested as a very sensitive method for the detection of small airways disease (6). In our subjects only one showed an abnormal washout curve and the same subject had frequency dependence of dynamic compliance. The lack of significant difference before and after smoke indicated that, at least in our hands, this method was not sensitive enough to detect the effects of acute inhalation.

The single-breath nitrogen washout has been recently introduced as a method of measuring "closing volume" (1). Closing volume (CV) represents the lung volume at which the airways in the dependent parts of the lung start closing (1, 5, 10). CV has been found to correlate well with age and smoking history (1, 18). Since airway closure occurs at collapsing transmural pressures, (1, 10) changes in the tonus of the bronchial wall could affect the "closing volume." We found no significant change in closing volume in 18 subjects before and after smoking. This might be due to lack of significant change in the bronchomotor tonus in the bronchi that close at CV. On the other hand, the deep inspiration preceding this procedure might have abolished the bronchoconstrictor effect of the cigarette (24).

The maximum expiratory flow-volume (MEFV) curve shows a drop in midexpiratory range and assumes a concave shape. Since lung compliance remained unchanged in our subjects, reduction of the MEF_{50} is probably the result of increased resistance of the upstream segment, because maximum expiratory flow is determined by elastic recoil of the lung and by the resistance of the airways situated upstream from the flow-limiting segment (21). Since the flow-limiting segment is usually in the lobar or segmental bronchi (21), in addition to the small airways a significant portion of the larger airways is upstream from it. Narrowing of bronchi upstream from the flow-limiting segment and greater than 2 mm in diameter could be responsible for the reduction in flow, rather than the increase in "true" small airway (less than 2 mm in diameter) resistance. This suggestion is further supported by the lack of change in MEF_{75}. If bronchoconstriction would occur in the "small airways," terminal flow would be equally reduced.

Both the large and small airways are probably affected by the acute inhalation of cigarette smoke causing a decrease of airway conductance and maximum expiratory flow at 50% of the vital capacity. No significant difference in response between smokers, nonsmokers, and subjects with chronic bronchitis was noted. Evidence of increased resistance in the "upstream" segment was found, but whether the "small airways" (less than 2 mm in diameter) are also contributing to the increased resistance has not been conclusively proven. It might be necessary to redefine the demarkation between "small" and "large" airways in more functional terms.

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